DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 16 2005

Ms. Susan Leonard
Regulatory Affairs Manager
Axis-Shield Diagnostics Ltd.
The Technology Park
Dundee, Tayside, Scotland
United Kingdom DD21XA

Re: k042411
Trade/Device Name: IMx® Sirolimus Microparticle Enzyme Immunoassay,
IMx® Sirolimus Calibrators,
IMx® Sirolimus Controls
Regulation Number: 21 CFR 862.3840
Regulation Name: Sirolimus Test System
Regulatory Class: Class II
Product Code: NRP, LAS, DLJ

Dear Ms. Leonard:

This letter corrects our substantially equivalent letter of April 7,2005 regarding the cleared devices and their product codes. The original letter failed to mention the clearance of your calibrators and controls.

We have reviewed your Section 510(k) premarket notification of intent to market the devices referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

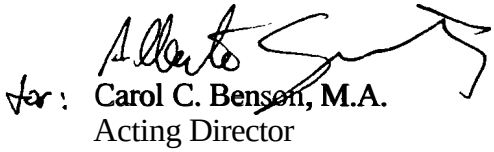
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



for: Carol C. Benson, M.A.
Acting Director
Division of Chemistry and Toxicology
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

3. INDICATIONS FOR USE

510(k) Number (if known): K042411

Device Name: IMx® Sirolimus Microparticle Enzyme Immunoassay

Indications For Use: The IMx® Sirolimus assay is an *in vitro* reagent system for the quantitative determination of sirolimus in human whole blood as an aid in the management of renal transplant patients receiving sirolimus therapy.

The IMx® Sirolimus Calibrators are for the calibration of the IMx Analyser when used for the quantitative determination of sirolimus in human whole blood.

The IMx® Sirolimus MODE 1 Calibrator is for the adjustment of the stored calibration of the IMx Analyser when used for the quantitative determination of sirolimus in human whole blood.

The IMx® Sirolimus Controls are for the verification of the calibration of the IMx Analyser when used for the quantitative determination of sirolimus in human whole blood.

The IMx® Sirolimus Whole Blood Precipitation Reagent is for the extraction of sirolimus from samples (whole blood patient specimens, IMx® Sirolimus Calibrators and Controls) to be tested on the IMx® Sirolimus assay.

Prescription Use ___√___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) **(21 CFR 807 Subpart C)**

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K042411

APR 7 2005

510(k) Summary

Introduction

The following summary is intended to support a claim for the Abbott IMx Sirolimus Assay of substantial equivalence to the Microgenics CEDIA Sirolimus Assay (K034069).

Submitter name, address, contact

Axis-Shield Diagnostics Ltd.
The Technology Park
Dundee DD2 1XA
Scotland, UK
Tel : +44 1382 422000
Fax: +44 1382 422088

Contact Person: Susan Leonard

Email address: susan_leonard@uk.axis-shield.com

Date Prepared: January 26th, 2005

Device Name

Proprietary Name: Abbott IMx® Sirolimus Microparticle Enzyme Immunoassay (MEIA) test

Common name: Microparticle Enzyme Immunoassay (MEIA) for the determination of sirolimus.

Classification name: Sirolimus test system

Product Code : NRP **Classification:** Class II CFR 862.3840

Predicate Device

This submission includes comparison of the IMx® Sirolimus assay to the currently accepted reference method for sirolimus measurement, which is High Performance Liquid Chromatography-tandem Mass Spectrometry (HPLC/MS/MS). There is also a comparison of performance characteristics for the IMx® Sirolimus Assay and the Microgenics CEDIA® Sirolimus Assay (K034069).

510(k) Summary

Device Description

Competition format.
Microparticle Enzyme Immunoassay (MEIA) for use on Abbott IMx® system.

Assay procedure:

- Incubate the sample with the anti-sirolimus antibody-coated microparticles.
- Add sirolimus alkaline phosphatase conjugate and incubate.
- Transfer to matrix cell.
- Wash to remove unbound substances.
- Add substrate.
- Measure fluorescent product.

Intended Use

An in vitro reagent system for the quantitative determination of sirolimus in human whole blood, as an aid in the management of renal transplant patients receiving sirolimus therapy.

Comparison to HPLC/MS/MS Method

The Abbott IMx Sirolimus assay was compared to the HPLC/MS/MS method. The resulting Passing-Bablok correlation statistics are summarised in the following table:

Clinical Site	Method X		Method Y		n	Min X	Max X	Min Y	Max Y	Passing / Bablok		r	Disp. of Residuals	
	Instrument	Unit	Instrument	Unit						B/P b	B/P a		md(68)	md(95)
All Samples														
All Sites	LC/MS/MS	ng/ml	IMx	ng/ml	221	2.900	90.100	3.800	81.900	1.230	-0.250	0.956	1.057	2.745

510(k) Summary

Performance Characteristics of Abbott IMx® Sirolimus MEIA Test vs the Microgenics CEDIA® Sirolimus Test:

Parameter	IMx® Sirolimus MEIA Test	CEDIA® Sirolimus Test (K034069)
Precision	Total imprecision of ≤ 15% through assay range of 5-22ng/ml	Within-run CV of 2.2 – 7.0%. Between-run CV of 2.2 – 9.2%.
Recovery	Mean recovery across samples of 90 – 110% of expected values.	Recovery of 101 – 112% of expected values.
Dilution Linearity	Mean recovery across samples of 99 – 115% of expected values.	Recovery of 91 – 106% of expected values for a single high sample.
Analytical Sensitivity	≤ 1.5ng/ml	4.0 ng/mL
Functional Sensitivity	≤ 2.5ng/ml	Not listed.
Specificity for Parent Compound	Cross-reactivity seen at the following levels with the metabolites studied: 11-hydroxy-sirolimus – 37% 41-O-demethyl-sirolimus – 58% 7-O-demethyl-sirolimus – 63% 41-O-demethyl-hydroxyl-sirolimus – 6%	Cross-reactivity seen at the following levels with the metabolites studied: 11-hydroxy – 44% 41-O- and 32-O -Demethyl – 73% Trihydroxy and 41-O-didemethyl – 14% 41-desmethyl-hydroxy- 10% Fraction 2 and 7-O-desmethyl – 8.7% Isomers of fraction 4 – 22% Hydroxyl – 7% N-oxide – 15% Fraction 6 and isomers of Fraction 7 – 4%

510(k) Summary

Performance Characteristics of Abbott IMx® Sirolimus MEIA Test (continued):

Parameter	IMx® Sirolimus MEIA Test	CEDIA® Sirolimus Test (K034069)
Co-Administered Drug Interference	62 drugs tested. Of these, the following showed between 10% and 15% apparent interference with the Medium Control: Gemfibrozil (75µg/ml) ; Itraconazole (10.5µg/ml) ; MPAG (1800µg/ml) ; OKT3(6.0µg/ml) ; Trimethoprim (40µg/ml).	42 drugs tested. These showed <0.015% cross-reactivity. 3 co-administered immunosuppressants tested: Cyclosporine at 10,000ng/ml, Tacrolimus at 300ng/ml, Mycophenolic Acid at 100,000ng/ml. Tacrolimus showed 0.4% cross-rectivity. Others showed <0.015% cross-reactivity.
Interference from Endogenous Compounds	≤ 10% interference in detecting sirolimus at the following levels of potentially interfering substances: Bilirubin – 0.4mg/ml Cholesterol – 5mg/ml Triglycerides – 10mg/ml Uric Acid – 0.2mg/ml Rheumatoid Factor – 500IU/ml Protein (Albumin) – 3-12g/dl Protein (Gamma Globulin) – 3-12g/dl HAMA – 60ng/ml Haematocrit levels between 15-60% produced <25% interference in the detection of sirolimus.	No significant interference from : Unconjugated bilirubin up to 60mg/dl Cholesterol up to 500mg/dl Triglycerides up to 1500mg/dl Rheumatoid Factor up to 573IU/ml Protein (albumin) up to 11g/dl Protein (gamma globulin) up to 4.9g/dl Haematocrit levels between 20 – 60% produced no significant interference.
Sample Storage / Stability	Specimens collected in EDTA tubes may be stored for up to 28 days at 2-8^{0}C or -20^{0}C prior to being tested. Repeated freezing and thawing (more than 3 freeze-thaw cycles) should be avoided.	1 week at 2-8°C and 2 years at -70°C.